DESCRIPTION

NOVEL COMPOUNDS FOR TREATMENT OF CARDIAC
ARRHYTHMIA, SYNTHESIS, AND METHODS OF USE

Cross-Reference to Related Application(s)

This application is a continuation application of co-pending application Serial
Now US 6,710,070,
No. 10/319,073, filed December 10, 2002; which claims the benefit of provisional
patent application Serial No. 60/339,898, filed December 10, 2001, which is hereby
incorporated by reference in its entirety.

Background of Invention

Congestive heart failure (CHF) is a disease affecting approximately 2% of the
population of the United States (Sami, M.H. [1991], J. Clin. Pharmacol. 31:1081).
Despite advances in the diagnosis and treatment of CHF, the prognosis remains poor
with a 5-year mortality rate higher than 50% from the time of diagnosis (McFate
Smith, W. [1985] Am. J. Cardiol. 55:3A; McKee, P.A., W.P. Castelli, P.M.
McNamara, W.B. Kannel [1971] N. Engl. J. Med. 285:1441). In patients with CHF,
the rate of survival is lowest in those patients with severe depression of left
ventricular function and patients who have frequent ventricular arrhythmias. Patients
with ventricular arrhythmias and ischemic cardiomyopathy have an increased risk of
sudden death. The presence of ventricular tachycardia in patients with severe CHF
results in a three-fold increase in sudden death compared to those without tachycardia
(Bigger, J.T., Jr. [1987] Circulation 75 (Supplement IV):28). Because of the high
prevalence of sudden unexpected death in patients with CHF, there has been a
growing interest in the prognostic significance of arrhythmias in these patients.

Several compounds have been used in the management of cardiac arrhythmias
in patients with congestive heart failure. Unfortunately, anti-arrhythmic drug therapy
has been disappointing. The efficacy of anti-arrhythmic drugs markedly decreases as
left ventricular function declines, such that only a small fraction of patients with CHF
are responsive to anti-arrhythmic therapy. No anti-arrhythmic drug has prevented